

1. (Currently amended) A method for assessing immune response profiles of animal populations comprising in operable combination the steps of:

- a) obtaining:
 - i) dendritic monocyte cells and CD4+ T-cells from an individual within said animal population, and
 - ii) and at least one protein sequence of interest;
- b) producing peptides comprising fragments of said protein sequence of interest, such that the entire protein sequence of interest is encompassed in said fragments;
- c) differentiating said dendritic monocyte cells to produce differentiated dendritic cells;
- d) exposing said peptides to said CD4+ T-cells and said differentiated dendritic cells;
- e) assessing the proliferation response of said CD4+ T-cells to each peptide; and
- f) determining the stimulation index of said proliferation response of said CD4+ T-cells to each of said peptides;
- g) repeating steps a) to f) for at least one additional individual;
- h) comparing the results for said individual and said at least one additional individual, such that the immune response of multiple individuals is provided; and
 - i) further performing a validation assay comprising determining proliferation of unfractionated peripheral blood mononuclear cells in response to the whole protein sequence of interest.

2. (Previously presented) The method of Claim 1, wherein a stimulation index of at least about 1.5 is recorded as positive.

3. (Previously presented) The method of Claim 1, wherein said animal population is a human population.

4. (Currently amended) The method of Claim 3, wherein the structure values of the responses observed for individuals within the population are determined using the formula:

$$\sum \left| f(i) - \frac{1}{p} \right|$$

wherein f(i) is the frequency of responses for an individual peptide and p is the number of peptides.

5. (Previously presented) The method of Claim 4, wherein said steps a) through h) are repeated using at least one additional protein of interest.

6. (Previously presented) The method of Claim 5, wherein said structure values of the responses for said protein of interest and said at least one additional protein of interest are used to rank the relative immunogenicity of said protein of interest and said at least one additional protein of interest.

7. (Previously presented) The method of Claim 6, wherein the protein having the lower structure value is ranked as being less immunogenic than a protein having a higher structure value.

8. (Previously presented) The method of Claim 5, wherein said at least one additional protein of interest comprises said protein of interest that has been modified to produce a modified protein of interest.

9. (Previously presented) The method of Claim 8, wherein said modified protein of interest is selected from the group consisting of hypoimmunogenic proteins and hyperimmunogenic proteins.

10. (Previously presented) The method of Claim 8, wherein said modified protein of interest is produced by substituting at least one amino acid in said at least one additional protein of interest to produce a variant protein of interest.

11. (Previously presented) The method of Claim 6, wherein said protein of interest and said at least one additional protein of interest are selected from the group of proteins consisting of enzymes, antibodies, soluble receptors, fusion proteins, structural proteins, binding proteins, and hormones.

12. (Previously presented) The method of Claim 9, wherein said enzyme is selected from the group consisting of proteases, subtilisins, cytokines, lipases, cellulases, amylases, oxidases, isomerases, kinases, phosphatases, lactamases, and reductases.

13-37. (Canceled)

38. (Currently amended) A method for determining the immune response of a test population against a test protein, comprising the following steps in operable order:

- (a) preparing a pepset set of peptides from a test protein;
- (b) obtaining a plurality of solutions comprising human dendritic monocyte cells and a plurality of solutions of naïve human CD4+ and/or CD8+ T-cells, wherein said solutions of human dendritic monocyte cells and solutions of naïve human CD4+ and/or CD8+ T-cells are obtained from a plurality of individuals within said test population;
- (c) differentiating said dendritic monocyte cells to produce a plurality of solutions comprising differentiated dendritic cells;
- (d) combining said plurality of solutions of differentiated dendritic monocyte cells and said solutions of naïve CD4+ and/or CD8+ T-cells with said

pepset set of peptides, wherein each of said solutions of differentiated dendritic cells and naïve CD4+ and/or CD8+ T-cells are from one individual within said test population are combined;

- (e) measuring proliferation of said T-cells in step (d), to determine the responses to each peptide in said pepset set of peptides;
- (g) compiling the responses of said T-cells in step (e) for said test protein;
- (h) determining the structure value of said compiled responses obtained in step (g) for said test protein using the formula:

$$\sum \left| f(i) - \frac{1}{p} \right|$$

wherein f(i) is the frequency of responses for an individual peptide and p is the number of peptides in the peptide set; and

- (i) determining the level of exposure of said plurality of individuals to said test protein; and
- (j) further performing a validation assay comprising determining proliferation of unfractionated peripheral blood mononuclear cells in response to whole test protein.

39. (Previously presented) The method of Claim 38, wherein said pepsets comprise peptides of about 15 amino acids in length.

40. (Previously presented) The method of Claim 39, wherein said peptides overlap each adjacent peptide by about 3 amino acids.

41. (Previously presented) The method of Claim 38, wherein said test protein is selected from the group of proteins consisting of enzymes, antibodies, soluble receptors, fusion proteins, structural proteins, binding proteins, and hormones.

42. (Previously presented) The method of Claim 38, wherein said enzyme is selected from the group consisting of proteases, subtilisins, cytokines, lipases, cellulases, amylases, oxidases, isomerases, kinases, phosphatases, lactamases, and reductases.

43. (Previously presented) The method of Claim 38, wherein the exposure level of said plurality of individuals to said test protein is compared.

44. (Previously presented) The method of Claim 38, further comprising at least one additional test protein.

45. (Previously presented) The method of Claim 44, wherein said at least one additional test protein is obtained by modifying said test protein.

46. (Previously presented) The method of Claim 44, wherein the background percent response and structure values of said test protein and said at least one additional test protein are categorized and/or ranked.

47. (Canceled)